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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,627	09/14/2001	Luigi Naldini	131.14-US-WO	5935

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EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 03/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,627	NALDINI ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-8* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed on 11-23-2004 are acknowledged. Claims 1-3 have been amended. Claims 4-8 have been added.

Newly submitted claim 8 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claim 8 is drawn to a method of detecting envelope defective retroviruses whereas the elected invention is drawn to a method of amplifying an envelope defective virus.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 8 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Consequently claims 1-7 are currently under examination.

Claim Rejections Withdrawn

Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The rejection of claim 1 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "exposing" is withdrawn in light of the amendment thereto.

The rejection of claim 2 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the phrase "wherein said virus envelope

protein is expressed at the surface of a virus particle produced by said cell" is withdrawn in light of the amendment thereto.

Claim Rejections Maintained

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-16 of U.S. Patent No. 5,994,136 for the reasons set forth in the previous Office action in the rejection of claims 1-3. Contrary to Applicant's assertion, the amendments to the instant claims are not sufficient to over come the instant rejection.

As outlined previously, although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. The instant claims are drawn to methods of amplifying (propagating) an envelope defective retrovirus by contacting said retrovirus to a cell that comprises a gene that encodes a virus envelope

integrated into its genome wherein said envelope gene complements said retrovirus. The instant claims have been amended to recite the limitation that said envelope gene is integrated into the cell's genome. Newly added claims recite the limitations that the envelope protein is VSVG (claim 4); that the retrovirus comprises an immunodeficiency virus, generally (claim 5) and HIV specifically (claim 6); and that the envelope gene is controlled by an inducible promoter. Moreover, while the instant claims require that the envelope gene be integrated, there is no requirement as to when said integration occurs. Consequently the instant claims only require that the envelope defective virus is amplified (claim 1), that the propagated virus comprises the envelope encoded by the integrated gene within the cell and that said envelope is expressed by said cell.

Patent 5,994,136 recites in the aforementioned claims methods for producing recombinant HIV vectors (an immunodefiency retrovirus) wherein a cell is transformed with an HIV packaging plasmid (i.e. an envelope defective retrovirus) and an expression plasmid encoding an envelope gene. The expression vector allows the cell to express envelope proteins on their membrane surfaces. Hence, when the HIV vector is expressed the resulting "envelope defective retrovirus" is "exposed" to a cell comprising a virus envelope gene. Moreover, since said virus envelope proteins encoded by said gene will be expressed on the cell surface, the "progeny" virus will have said envelope proteins on its surface since the replication cycle of retroviruses includes budding through the cell membrane of the infected cell. Moreover, U.S. Patent No. 5,994,136 discloses that the transgenes are integrated (see column 8, lines 47-48), that VSVG can be used as the env gene (see column 3, lines 47-50 and column 4, lines 1-3), and that the env gene be controlled by an inducible promoter (see column 4, lines 4-5). Consequently, claims 13-

16 of U.S. Patent No. 5,994,136 anticipate, and hence render obvious, the rejected claims since the disclosure clearly contemplates the specific embodiments recited in the instant claims.

Claims 1-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-9 of U.S. Patent No. 6,428,953 for the reasons set forth in the previous Office action in the rejection of claims 1-3. Contrary to Applicant's assertion, the amendments to the instant claims are not sufficient to over come the instant rejection.

As outlined previously, although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. The instant claims are drawn to methods of amplifying (propagating) an envelope defective retrovirus by contacting said retrovirus to a cell that comprises a gene that encodes a virus envelope integrated into its genome wherein said envelope gene complements said retrovirus. The instant claims have been amended to recite the limitation that said envelope gene is integrated into the cell's genome. Newly added claims recite the limitations that the envelope protein is VSVG (claim 4); that the retrovirus comprises an immunodeficiency virus, generally (claim 5) and HIV specifically (claim 6); and that the envelope gene is controlled by an inducible promoter. Moreover, while the instant claims require that the envelope gene be integrated, there is no requirement as to when said integration occurs. Consequently the instant claims only require that the envelope defective virus is amplified (claim 1), that the propagated virus comprises the envelope encoded by the integrated gene within the cell and that said envelope is expressed by said cell.

Patent 6,428,953 recites in the aforementioned claims methods for producing recombinant HIV vectors (an immunodefiency retrovirus) wherein a cell is transformed with an HIV packaging plasmid (i.e. an envelope defective retrovirus) and an expression plasmid encoding an envelope gene. The expression vector allows the cell to express envelope proteins on their membrane surfaces. Hence, when the HIV vector is expressed the resulting "envelope defective retrovirus" is "exposed" to a cell comprising a virus envelope gene. Moreover, since said virus envelope proteins encoded by said gene will be expressed on the cell surface, the "progeny" virus will have said envelope proteins on its surface since the replication cycle of retroviruses includes budding through the cell membrane of the infected cell. Moreover, U.S. Patent No. 6,428,953 discloses that the transgenes are integrated (see column 8, lines 49-50), that VSVG can be used as the env gene (see column 3, lines 53-55 and column 4, lines 5-7), and that the env gene be controlled by an inducible promoter (see column 4, lines 8-9). Consequently, claims 13-16 of U.S. Patent No. 6,428,953 anticipate, and hence render obvious, the rejected claims since the disclosure clearly contemplates the specific embodiments recited in the instant claims.

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3 and 5-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Sadaie et al. (Virology, 1992, Vol. 187, pages 604-611) for the reasons outlined in the previous Office action in the rejection of claims 1-3.

Applicant argues the amendments to the instant claims renders the aforementioned rejection moot.

Applicant's arguments have been fully considered and deemed non-persuasive.

The instant claims are drawn to methods of amplifying (propagating) an envelope defective retrovirus by contacting said retrovirus to a cell that comprises a gene that encodes a virus envelope integrated into its genome wherein said envelope gene complements said retrovirus. The instant claims have been amended to recite the limitation that said envelope gene is integrated into the cell's genome. Newly added claims recite the limitations: that the retrovirus comprises an immunodeficiency virus, generally (claim 5) and HIV specifically (claim 6). Moreover, while the instant claims require that the envelope gene be integrated, there is no requirement as to when said integration occurs. Consequently the instant claims only require that the envelope defective virus is amplified (claim 1), that the propagated virus comprises the envelope encoded by the integrated gene within the cell and that said envelope is expressed by said cell.

As outlined previously, Sadaie et al. disclose the production of an envelope defective HIV-1 virus and Env-producing plasmids (see abstract and materials and methods section on page 605). Sadaie et al. further disclose that the defective virus and the Env-producing plasmid is transfected into cells (see methods section on page 605). Said transfected cells produce virus particles with the wild-type phenotype (i.e. viruses have an envelope) [see page 607, 2nd column]. Moreover, since the progeny virus has the wild-type phenotype, it is apparent that the envelope proteins encoded by envelope "gene" is expressed on the cell surface since the replication cycle of retroviruses includes budding through the cell membrane of the infected cell. Consequently, Sadaie et al. anticipates all the limitations of the instant claims.

Claims 1-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Naldini et al. (U.S. Patent No. 5,994,136) for the reasons set forth in the previous Office action in the rejection of claims 1-3.

Applicant argues the amendments to the instant claims renders the aforementioned rejection moot. Applicant's arguments have been fully considered and deemed non-persuasive.

The instant claims are drawn to methods of amplifying (propagating) an envelope defective retrovirus by contacting said retrovirus to a cell that comprises a gene that encodes a virus envelope integrated into its genome wherein said envelope gene complements said retrovirus. The instant claims have been amended to recite the limitation that said envelope gene is integrated into the cell's genome. Newly added claims recite the limitations that the envelope protein is VSVG (claim 4); that the

retrovirus comprises an immunodeficiency virus, generally (claim 5) and HIV specifically (claim 6); and that the envelope gene is controlled by an inducible promoter. Moreover, while the instant claims require that the envelope gene be integrated, there is no requirement as to when said integration occurs. Consequently the instant claims only require that the envelope defective virus is amplified (claim 1), that the propagated virus comprises the envelope encoded by the integrated gene within the cell and that said envelope is expressed by said cell.

Patent 5,994,136 recites in the aforementioned claims methods for producing recombinant HIV vectors (an immunodefiency retrovirus) wherein a cell is transformed with an HIV packaging plasmid (i.e. an envelope defective retrovirus) and an expression plasmid encoding an envelope gene. The expression vector allows the cell to express envelope proteins on their membrane surfaces. Hence, when the HIV vector is expressed the resulting "envelope defective retrovirus" is "exposed" to a cell comprising a virus envelope gene. Moreover, since said virus envelope proteins encoded by said gene will be expressed on the cell surface, the "progeny" virus will have said envelope proteins on its surface since the replication cycle of retroviruses includes budding through the cell membrane of the infected cell. Moreover, U.S. Patent No. 5,994,136 discloses that the transgenes are integrated (see column 8, lines 47-48), that VSVG can be used as the env gene (see column 3, lines 47-50 and column 4, lines 1-3), and that the env gene be controlled by an inducible promoter (see column 4, lines 4-5). Consequently, claims 13-16 of U.S. Patent No. 5,994,136 anticipate, and hence render obvious, the rejected claims since the disclosure clearly contemplates the specific embodiments recited in the instant claims.

Claims 1-5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Ory et al. (PNAS, 1996, Vol. 93, pages 11400-11406 – IDS-8) for the reasons set forth in the previous Office action in the rejection of claims 1-3.

Applicant argues the amendments to the instant claims renders the aforementioned rejection moot. Applicant's arguments have been fully considered and deemed non-persuasive.

The instant claims are drawn to methods of amplifying (propagating) an envelope defective retrovirus by contacting said retrovirus to a cell that comprises a gene that encodes a virus envelope integrated into its genome wherein said envelope gene complements said retrovirus. The instant claims have been amended to recite the limitation that said envelope gene is integrated into the cell's genome. Newly added claims recite the limitations: that the envelope protein is VSVG (claim 4); that the retrovirus comprises an immunodeficiency virus; and that the envelope gene is controlled by an inducible promoter. Moreover, while the instant claims require that the envelope gene be integrated, there is no requirement as to when said integration occurs. Consequently the instant claims only require that the envelope defective virus is amplified (claim 1), that the propagated virus comprises the envelope encoded by the integrated gene within the cell and that said envelope is expressed by said cell.

As outlined previously, Ory et al. disclose a packaging cell line for the production of high titer retroviruses with VSV G protein (envelope protein) [see abstract]. Ory et al. further disclose the transfecting of cells with a retroviral vector (MuMLV-Env defective) and a plasmid encoding VSV-G envelope protein (see page 11401, 1st column and page

11403). Ory et al. further disclose the use of an inducible promoter to regulate the expression of the VSVG envelope protein (see page 11402, 1st column). Ory et al. also disclose that said cells expressed VSV-G on its surface (see page 11401, 2nd column and page 11403). The resulting "psuedotypes" (i.e. viruses produced by the transfected cells) contain VSV-G envelope proteins on their surface (see pages 11405-11406). Consequently, Ory et al. anticipates all the limitations of the rejected claims.

New Grounds of Rejection

35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is rendered vague and indefinite by the use of the term "carried by a virus particle". It is unclear what is meant by said term since it is not explicitly defined in the specification. Is said limitation meant to include anything other than the recited envelope protein to serve as the viral envelope for the virus particles produced by said indicator cell line? As written, it is impossible to determine the metes and bounds of the claimed invention.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert A. Zeman
February 22, 2005

L. F. Smith
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